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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,864	11/24/2000	David Scheinberg	D6126	4077

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,864	SCHEINBERG ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 1, 3, 7 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 103, NEW REJECTION

Claims 1, 3, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonson et al, 1990, Cancer Res, 50 (3 Supp): 9855-9885, of record, in view of Kasperson, FM et al, of record, US 4,665,897, of record, and US 6,197,278 or Vieira, MR, et al, 1996, Eur J Surgical Oncology, 22(4): 331-4, and further in view of US 4,444744A .

Claims 1, 3, 7 are drawn to a method of killing a tumor greater than 1 mm in size, comprising repeatly administering a construct comprising an alpha emitting isotope, and an antibody specific for said tumor, having a high specific activity from about 0.1 mCi/mg to about 30 mCi/mg, wherein said specific activity sufficient for a pharmacologically effective dose of said construct to provide an amount of antibody to bind to a plurality of the targeted sites on the tumor cells, wherein a minimum of one atom of said alpha particle-emitting isotope comprising said construct delivers at least one alpha track to the tumor cells upon binding of the antibody. Said alpha emitting isotope is bismuth-213, and, and is administered at a dose of about 0.1 mg/m^2 to about 10 mg/m^2.

Simonson et al teach i.p. administration of 212-Bi labeled antibodies specific for the mucin antigen TAG-72 into mice previously injected with LS1744T cells which grow both as solid tumors and ascites in mice, wherein the mice develop ascites at about 20 days after injection of the tumor cells (p. 985s, second column, last paragraph), and only after the development of solid tumor (p. 987s, second column, first paragraph). Simonson et al teach that the specific activity of the labeled antibody is 5 to 10 uCi/ug (p.986s, first column, second paragraph), which is the same as 5 to 10 mCi/mg and is within the range of the claimed specific activity. Simonson et al further teach that for advanced tumors of 13 days after injection of tumor cells, with single and repeated administration of Bi-212 labeled antibody, 56% decrease in tumor mass is obtained (p.986s, first column, third paragraph and figure 1 on page 986s). Simonson et al teach that 13 days after injection, the tumor mass is 3 gm on average (figure 1). Simonson et al teach that the efficacy of the treatment would be even better if the radiolabeled antibody recognizes an antigen on cell surface of target cell, rather than the mucin antigen TAG-72, which is secreted (p.987s, second column).

Simonson et al do not teach a method of killing a tumor greater than 1 mm in size, comprising intravenously administering antibodies that are labeled with Bi-213, at a dose adequate to deliver a minimum of 1 alpha track per cell, or at a dose of about 0.1 mg/m^2 to about 10 mg/m^2.

Kaspersen et al teach that Bi-213 can be an alternative to Bi-212, with the advantage of safer and easier production (p.475, first column, first paragraph).

US 4,665,897 teach a method of treating tumors comprising administering antibodies containing inactive nuclide that could be rendered radioactive with externally generated radiation, wherein the steps of said method are repeated as many times as necessary to effect remission or destruction of tumors (Claims 28, 35, 36). Said radiation includes alpha particles (claim 27).

Vieira, MR, et al teaches that imaging of breast cancer tissues could begin 10 minutes after intravenous administration of radiolabeled monoclonal antibodies. In other words, radiolabeled monoclonal antibodies could reach the breast cancer tissues within minutes after its intravenous administration.

US 6,197,278 teaches that after i.v. administration, localization of a radiolabeled targeting protein, annexin, a protein having high affinity for anionic phospholipid surface, in the target tissue can be obtained in only a few minutes (columns 9-10, especially last two paragraphs of column 9, bridging column 10).

US 4,444744A teaches use of radiolabeled antibodies to cancer cell surface antigens for cancer immunotherapy.

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to treat tumors of at least 1 mm in size using the method of Simonson et al, comprising administering an antibody labeled with Bi-212. Although Simonson et al do not teach that the treated tumors are at least 1 mm in size, one would have expected that the size of the solid tumors taught by Simonson et al would be at least 1 mm in size, because the solid tumors taught by Simonson et al have 3gm average in weight, and are advanced tumors after 13 days of growth.

It would have been obvious to substitute Bi-212 with Bi-213, because Bi-213 has the advantage of safer and easier production, as taught by Kasperson et al.

It would have been obvious to replace antibodies specific for the mucin antigen TAG-72 taught by Simonson et al, which, although is found in many adenocarcinoma, but is a secreted antigen, with an antibody that targets a membrane cancer specific antigen on cancer cells, as suggested by Simonson et al, because an antibody to a cancer membrane antigen would be more effective than an antibody to a secreted antigen for targeting a cancer cell, and because antibodies specific for cancer specific antigens on cancer cell surface for use in cancer immunotherapy are well known in the art, as taught by US 4,444744A .

It would have been obvious to administer the labeled antibody intravenously, because it is a routine route of administration of labeled antibodies for immunotherapy.. One would have expected that the Bi-212 or Bi-213 radiolabeled antibody would reach the target cancer cells within minutes after its intravenous administration, and that the Bi-212 or Bi-213 radiolabeled antibody would have ample time to kill target cancer cells, despites the relative short half life of Bi-212 or Bi-213, because targeting compounds, such as radiolabeled antibody, or annexin, have been shown to be able to reach the target cancer cells within minutes after their intravenous administration, as taught by Vieira, MR, et al and US 6,197,278.

It would have been obvious to administer the labeled antibody once or repeatly, as taught by Simonson et al, and US 4,665,897, to ensure destruction of the tumors.

With regards to the dosage of the labeled antibodies recited in claims 1, 7, to determine optimum dosage is within the level of ordinary skill in the art. See In re Kronig, 190 USPQ 425.

One of ordinary skill in the art would have been motivated to treat tumors having at least 1mm in size using an antibody labeled with Bi-213, that targets a specific binding site on tumor cells, with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

October 02, 2004